

# Surgical management of thyroid follicular neoplasms: A retrospective analysis of 128 patients

Surgical management of thyroid follicular neoplasms

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Aim: The most appropriate surgical management of follicular neoplasm/suspicious for follicular neoplasm (FN) lesions is still controversial. The aim of the study is to analyze the outcomes of surgical procedures in the treatment of FN patients. Material and Method: We retrospectively evaluated 128 patients, surgically treated after an FN diagnosis. Total thyroidectomy (TT) or hemithyroidectomy (HT) was performed according to the clinical signs of the patients. The main criteria for HT were a single nodule, nodule size, younger age, and the absence of thyroiditis or clinical/intraoperative suspicion of malignancy. Age, gender, associated thyroiditis, and nodule size were compared along with definitive pathology. Complication rates were also evaluated. Results: TT was performed in 87/128 (68%) and HT in 41/128 (32%) patients. Completion thyroidectomy was required in only 6/41 HT patients. The overall malignancy rate was 37/128 (28.9%); 32.4% (12/37 patients) following HT, and 67.6% (25/37 patients) following TT, respectively. No complications were reported in the HT group. Discussion: Considering the low risk of FN lesions, HT is an appropriate method for treatment in selected patients with minimal morbidity. However, in cases of multinodular disease, associating chronic thyroiditis, or a higher risk of cancer, TT should be recommended.

### Keywords

Follicular Neoplasm; Suspicious For Follicular Neoplasm; Hemithyroidectomy; Total Thyroidectomy

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#### Introduction

With the extensive use of thyroid ultrasonography (US) and US guided fine needle aspiration cytology (FNAC) in thyroid pathologies, we encounter 15-30% of cases of "follicular neoplasm/ suspicious for follicular neoplasm" lesions (FN) [1-4]. However, we also know that preoperative US features, molecular markers, or intraoperative consultation [5] are not accurate enough to predict malignancy. Usually, identification of capsular or vascular invasion is necessary to achieve a definitive diagnosis. Therefore, less frequently, papillary thyroid carcinoma (PTC), typically in its follicular variant (FVPTC) and, even rarer, follicular thyroid carcinoma (FTC), may be diagnosed postoperatively [1].

The increased number of FN diagnoses has led to more thyroid surgical procedures, demonstrating that malignancy rate associated with FN is low (10-30%) [6,7]. On the other hand, in several patients who underwent lobectomy, a completion thyroidectomy was required. Despite several studies, management guidelines are controversial. Hemithyroidectomy (HT) was considered as an adequate procedure in 96% of FN cases [8]. On the contrary, the frequent presence of a contralateral occult microcarcinoma, the increased healthcare costs in managing the remnant lobe, and increasing complication rates of re-interventions are the main arguments in favor of total thyroidectomy (TT) [9-12]. Current literature confirms the need for better preoperative evaluation of patients with FN to avoid unnecessary diagnostic surgery.

The aim of this study is to analyze the outcomes of two surgical procedures, namely TT vs HT in the treatment of FN patients.

## Material and Method

We retrospectively analyzed 128 patients who were treated between January 2012 and May 2017 in the Endocrine Surgery Unit of Ankara Guven Hospital. Hemithyroidectomy was performed in 41/128 (32%) patients and the remaining 87/128 (68%) had the TT procedure. Two senior endocrine surgeons performed the operations and a single experienced pathologist performed the histopathological examinations. The Bethesda NCI Conference criteria for FN were adopted: a moderate/high cellularity and a microfollicular pattern with minimal or absent colloid background were the main diagnostic criteria. Conversely, cells with overlapping and crowding patterns, and/or nuclear atypia (vesicular nuclei, micro nucleoli, and irregular cell membrane), which raised the likelihood for PTC, were excluded. Age, gender, associated thyroiditis, and nodule size were compared along with definitive pathology. Pathological examination and surgical complications represent the main parameters of this analysis.

There were 96 females (75%), and 32 males (25%) with a mean age of 43.4 years (31 - 64 years) included in this study. A single nodule, younger age, the absence of thyroiditis, or radiological, clinical, and intraoperative suspicion of malignancy were the main criteria leading to HT vs TT. Frozen section examination was performed in 38/41 HT patients according to the associated risk factors. An intraoperative nerve monitoring was utilized after March 2014. Vocal cord paresis was considered permanent six months after surgery. Serum calcium levels were determined on post-operative day 1 in only TT group. Patients were

discharged without levothyroxine replacement in the HT group and thyroid function tests were completed 4-6 weeks later.

#### Statistical analysis

All data are expressed as mean or as percentage.

#### Results

Malignancy was diagnosed in 37/128 (28.9%) patients; 12/37 patients following HT, and 25/37 patients following TT patients, respectively.

PTC was found in 28/37 (75.7%) of the cases; most of them were FVPTC (18/28 patients) and 20/28 were microcarcinomas. FTC was diagnosed in 6/37 (16.2%) patients, whereas 3/37 (8.1%) cases were well-differentiated thyroid tumors of uncertain malignant potential (WDT-UMP). Follicular adenoma, nodular hyperplasia, and chronic thyroiditis were diagnosed in 55/128 (43%), 29/128 (22.7%), and 7/128 (5.4%) patients, respectively (Table 1).

Chronic thyroiditis co-existed in 7/128 (5.46%) of all patients, and only 4/37 of the cases were associated with cancer (10.8%). Factors associated with malignancy were age, gender, and nodule size. Factors associated with malignancy are documented in Table 2.

Complication rates are presented in Table 3. Permanent RLN paralysis or hypocalcaemia were not observed in either group. However, transient RLN palsy was found in 2/87 (2.3%) of the TT patients but was not observed in the HT group. Transient hy-

Table 1. Histopathological features of HT and TT groups

	HT (n:12)	TT (n:25)
Papillary thyroid carcinoma	7 (58.3%)	21 (84%)
Follicular thyroid carcinoma	4 (33.3%)	3 (12%)
WDT-UMP	1 (8.3%)	1 (4%)
	HT (n:29)	TT (n:62)
Follicular adenoma	22 (75.9%)	33 (53.2%)
Nodular hyperplasia	4 (13.8%)	25 (40.3%)
Chronic thyroiditis	3 (10.3%)	4 (6.5%)

WDT-UMP: Well-differentiated thyroid tumor of uncertain malignant potential

Table 2. Comparison of HT and TT groups

		FN	
		HT (n=41)	TT (n=87)
Age		44.4	42.3
Gender	Female	30	66
	Male	11	21
Nodule size (mean)		7.8 mm (6-23 mm)	13.7 mm (3-36 mm)
Chronic thyroiditis	Yes	23 (56.1%)	4 (4.6%)
	No	18 (43.9%)	83 (95.4%)

Table 3. Surgical complications of two different surgical techniques.

		FN	
		HT (n=41)	TT (n=87)
RLN palsy	Transient	0 (0%)	2 (2.3%)
	Permanent	0 (0%)	0 (0%)
Hypoparathyroidism	Transient Permanent	1 (2.4%) 0 (0%)	4 (4.6%) O (0%)
	Permanent	0 (0%)	0 (0%)

RLN: recurrent larvngeal nerve

poparathyroidism was observed in 1/41 in the HT group (2.4%; 1/41) and 4/87 (4.6%) in the TT group.

Completion thyroidectomy was performed whenever pathology revealed malignancy on the HT surgical specimen, which was a microcarcinoma in 6/41 cases (14.6%). Transient hypocalcaemia that was observed in the HT group was one of the completion thyroidectomy cases.

All of the patients were discharged after 24 hours regardless of the surgical procedure.

#### Discussion

This study analyses the final histopathological results of FNAC diagnosis FN patients and compares the differences between the selected surgical procedures TT vs HT.

Risk factors such as age, gender, nodule size, serum thyroglobulin levels, US findings, molecular and genetic markers have been intensively investigated in the past for making management decisions. In the latest ATA guidelines, a more accurate US assessment was done in order to classify thyroid nodules [3,7,13]. Therefore, some immunocytochemical and genetic markers may be useful in order to discriminate benign adenomas from carcinomas, but these markers need to be validated in larger series [2,14-21]. The choice of the most suitable surgical procedure is also related to many additional parameters.

Nodular goiter is an endemic problem in most part of Turkey. The incidence of autoimmune diseases, in particular Hashimoto's thyroiditis, is also a common problem especially in Turkish women, probably determining a more elevated rate of malignant neoplasms, justifying the wide diffusion of TT. Therefore, the characteristics of the population at risk and the clinic-pathological features of cancer itself may be significantly different according to ethnicity and geographical location [22].

The overall malignancy rate of previously diagnosed FN patients is approximately 29% in our study. When we look at the subgroups; it is 67.6% and 32.4% in TT and HT groups, respectively. The two-fold increase in final histopathology cancer diagnosis in the TT group indicates an effective selection of

According to available data, both HT and TT maintain an important role in the current approach to thyroid neoplasms [23]. In case of small FN solitary, low-risk lesions, HT, that avoids the possibility of bilateral RLN palsy and lifelong L-thyroxine replacement therapy, may represent the most accurate procedure [24] and the safest standard of care [1]. TT may be an over-treatment in a high number of patients and should be considered carefully.

Revised ATA guidelines consider HT a sufficient treatment for incidental, small (<1 cm), low-risk, unifocal, intrathyroidal papillary carcinomas, in absence of clinical lymph nodes metastases [25]. In our series, completion thyroidectomy was required in only 6/41 (14.6%). Our series confirmed the absence of definitive complications, also following a completion thyroidectomy. Transient RLN paralysis was similar between the two groups while transient hypoparathyroidism rate was lower following HT.

The most effective surgical procedure following FN diagnosis is still controversial. In solitary, small, and low-risk lesions, HT is still the safest method of surgical treatment, avoiding unneces-

sary morbidity. Considering the low malignancy rate of these patients, HT may be a good option for such cases. TT should be recommended in cases of multiglandular disease or in the presence of thyroiditis that might be associated with a higher risk of cancer.

### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

### Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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#### Conflict of interest

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#### References

- 1. Conzo G, Troncone G, Docimo G, Pizza A, Sciascia V, Bellevicine C, et al. Cytologically undetermined follicular lesions: surgical procedures and histological outcome in 472 cases. Ann Ital Chir. 2013; 84(3): 251-6.
- 2. Troncone G, Volante M, Iaccarino A, Zeppa P, Cozzolino I, Malapelle U. Cyclin D1 and D3 overexpression predicts malignant behavior in thyroid fine-needle aspirates suspicious for Hurtle cell neoplasms. Cancer. 2009; 117(6): 522-9.
- 3. Baldini E, Sorrenti S, Di Gioia C, De Vito C, Antonelli A, Gnessi L. Cervical lymph node metastases from thyroid cancer: does thyroglobulin and calcitonin measurement in fine needle aspirates improve the diagnostic value of cytology? BMC Clin Pathol. 2013: 13(1): 7.
- 4. Calo P.G, Lai M.L, Guaitoli E, Pisano G, Favoriti P, Nicolosi A. Difficulties in the diagnosis of thyroid paraganglioma: a clinical case. La Clin Ter. 2013; 164(1): 35-9. 5. McHenry C.R, Raeburn C, Strickland T, Marty J.J. The utility of routine frozen section examination for intraoperative diagnosis of thyroid cancer. Am J Surg. 1996: 172(6): 658-61.
- 6. Smith J, Cheifetz R.E, Schneidereit N, Berean K, Thomson T. Can cytology accurately predict benign follicular nodules? Am J Surg. 2005; 189(5): 592-5.
- 7. Lee K.H, Shin J.H, Ko E.S, Hahn S.Y, Kim J.S, Kim J.H, et al. Predictive factors of malignancy in patients with cytologically suspicious for Hurthle cell neoplasm of thyroid nodules. Int J Surg. 2013; 11(9): 898-2.
- 8. Wiseman S.M. Baliski C. Irvine E. Anderson D. Wilkins G. Filipenko D. et al. Hemithyroidectomy: the optimal initial surgical approach for individuals undergoing surgery for a cytological diagnosis of follicular neoplasm. Ann Surg Oncol. 2006; 13(9): 425-32.
- 9. Docimo G, Ruggiero R, Gubitosi A, Casalino G, Bosco A, Gili S, et al. Ultrasound scalpel thyroidectomy: prospective randomized study. Ann Ital Chir. 2012; 83(4):
- 10. De Bellis A, Conzo G, Cennamo G, Pane E, Bellastella G, Collella C, et al. Time course of Grave's ophthalmopathy after total thyroidectomy alone or followed by radioiodine therapy: a 2-year longitudinal study. Endocrine. 2012; 41(2): 320-6.
- 11. Calo P.G, Pisano G, Piga G, Medas F, Tatti A, Donatti M. Postoperative hematomas after thyroid surgery. Incidence and risk factors in our experience. Ann Ital
- 12. Conzo G, Pasquali D, Bellastella G, Esposito K, Carella C, Bellis A, et al. Total thyroidectomy, without pro-phylactic central lymph node dissection, in the treatment of differentiated thyroid cancer. Clinical retrospective study on 221 cases. Endocrine. 2013; 44(2): 419-25.
- 13. Trimboli, S. Ulisse, M. D'Alo\_, F.Solari, A Fumarola, M.Ruggieri, et al. Analysis of clinical, ultrasound and colour flow-Doppler characteristics in predicting malignancy in follicular thyroid neoplasms. Clin Endocrinol. 2008; 69(48):342-4
- 14. Bartolazzi A, Orlandi F, Saggiorato E, Volante M, Arecco F, Rosetto R, et al. Galectin-3-expression analysis in the surgical selection of follicular thyroid nodules with indeterminate fine- needle aspiration cytology: a prospective multicen-

tre study. Lancet Oncol. 2008;9(6):543-549.

- 15. Finley D, Zhu B, Barden C.B, Fahey T. Discrimination of benign and malignant thyroid nodules by molecular profiling. Ann Surg. 2004; 240(3): 425-36.
- 16. Herrmann M.E, LiVolsi V.A, Pasha T.L, Roberts S.A, Wojcik E.M, Baloch ZW. Immunohistochemical expression of galectin-3 in benign and malignant thyroid lesions. Arch Pathol Lab Med. 2002; 126(6): 710-3.
- 17. Carpi A, Naccarato A.G, Iervasi G, Nicolini A, Bevilacqua G, Viacava P, et al. Large needle aspiration biopsy and galectin-3 determination in selected thyroid nodules with indeterminate FNA-cytology. Br J Cancer. 2006; 95(2): 204-9.
- 18. Mekel M, Nucera C, Hodin R.A, Parangi S. Surgical implications of BRafV600E mutation in fine-needle aspiration of thyroid nodules. Am J Surg. 2010; 200(1): 136-43.
- 19. Pasquali D, Santoro A, Bufo P, Conzo G, Deery W.J, Renzullo A, et al. Upregulation of endocrine gland-derived vascular endothelial growth factor in papillary thyroid cancers displaying infiltrative patterns, lymph node metastases, and braf mutation. Thyroid. 2011; 21(4): 391-9.
- 20. Conzo G, Docimo G, Pasquali D, Mauriello C, Gambardella C, Esposito D, et al. Predictive value of nodal metastases on local recurrence in the management of differentiated thyroid cancer. Retro- spective clinical study. BMC Surg. 2013; 13 Suppl 2: S3
- 21. Alexander E.K, Kennedy G.C, Baloch Z.W, Cibas E.S, Chudova D, Diggans J, et al. Preoperative diagnosis of benign thyroid nodules with indeterminate cytology. N Engl J. Med. 2012; 367(89): 705-15.
- 22. Lee S.H, Baek J.S, Lee JY, Lim JA, Cho SY, Lee TH, et al., Predictive factors of malignancy in thyroid nodules with a cytological diagnosis of follicular neoplasm. Endocr Pathol. 2013; 24(4): 177-83
- 23. Dobrinja C, Trevisan G, Piscopello L, Fava M, Liguori G. Comparison between thyroidectomy and hemithyroidectomy in treatment of single thyroid nodules identified as indeterminate follicular lesions by fine-needle aspiration cytology. Ann Ital Chir. 2010; 81(6): 403-10.
- 24. Antunes C.M, Taveira-Gomes A. Lobectomy in follicular thyroid neoplasms' treatment. Int J Surg. 2013; 11(9): 919-22.
- 25. Cooper D.S, Doherty G.M, Haugen B.R, Kloos R.T, Lee S.L, Mandel S.J, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2009: 19(11): 1167-14.

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